

SPL Process ER/DL Meeting

Meeting Minutes

April 5, 2017

Chair of today's meeting: Herb O'Brien

Teleconference information (Herb O'Brien):

USA : 412-777-7525

Conference ID: 502 567 562

Link to the SPL wiki:

<http://spl-work-group.wikispaces.com/share/view/51351516>

Agenda:

1. Announcement: Pat Cowall will be taking a voluntary package from Lilly and retiring on May 31, 2017. This came up very unexpectedly. It was a tough decision, but the package was too good and the timing was too perfect – summer and arrival of the first grandchild in mid July. Future plans are under development – probably a combination of consulting, volunteer work, family, ... and possibly coming to SPL meetings on Wednesdays.
2. Additional Comments by Gary Saner

Meeting discussion:

- Standards supporting IDMP: 2012 – Pharmaceutical and Medicinal Standards and implementation guides. Waiting for these to be updated.
- HL7: SPL version that can support IDMP data elements. SPL R7 included some. SPL R8 will be balloted this summer. EMA driven activity.
- FDA and IDMP: Implementation will be evolutionary. FDA already embedded some of the standards.
- IDMP has included 150 fields. FDA included about 50 fields.
- FDA may add some IDMP more over time...either by guidance or a binding guidance.
- NIH already has a group of developers looking at global need for identifying ingredients...G-SRS...that has been developed by a global group. Composite of many global repositories. Search for NIH and G-SRS.
- A number of mfg'ers are starting to work on IDMP and adopting into their plans.
- Later this year, EMA will be publishing SPOR (referential data) website available. Similar to EVMPD website. SPOR is redesign.
- 2019 mid/end – voluntary submissions. Then mandatory after 6 months.
- Marketplace: some tools/vendors are working on this – ie tools.
- There is an online database to enter manually.
- There is also a gateway to enter SPL format file.
- Software tools: 2 types of tools. IDMP data hub. More comprehensive solution RIM suite of tools – will include IDMP solutions.
- If want to get involved and learn more, join IRISS.

3. SPL Marketing Category Terminology Update

The marketing categories in third column of the table below will be replaced by the marketing categories in the first column. The marketing categories are posted on the FDA

SPL web page:

<https://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162528.htm>.

SPL Marketing Category Terminology Update			
Replacement		To Be Replaced	
Marketing Category Term	NCI Concept Code	Marketing Category Term	NCI Concept Code
Approved Drug Product Manufactured Under Contract	C132333	Approved Drug Product Manufactured Exclusively for Private Label Distributor	C95600
OTC Monograph Drug Product Manufactured Under Contract	C132334	OTC Monograph Drug Product Manufactured Exclusively for Private Label Distributor	C95601
Unapproved Drug Product Manufactured Under Contract	C132335	Unapproved Drug Product Manufactured Exclusively for Private Label Distributor	C95602

Questions from Group Members

1. **Has anyone had any experience with bulk packaging and drug listing? For example, we have a product which we manufacture in bottles of 60, 90 and 100 count as well as a box of 1,000 which goes to repackagers and never hits the shelf for commercial distribution. Does the box of 1,000 need to be drug listed as well or does the repacker simply use the source product code from the additional bottle counts and we do not have to include the box in our listing? Any help on this would be appreciated. The bulk container is not being imported. Jennifer Hinzman**

[HOB response and Meeting discussion:](#)

HOB:

- All registered establishments must list all of the products they produce for commercial distribution under their own labeler code. This includes API manufacturers, other bulk manufacturers, contract manufacturers, repackers, and relabelers.
- The product packaged in 1000 count box will be listed separately within the **Drug for further processing SPL** document (category under marketing) with the manufacturer's NDCs.
- The packager will need to drug list it with their NDCs once the product is packaged for commercial distribution. See below:
- Attached is the Bulk Ingredient SPL training slides provided by Lonnie. Hope this helps!

SUFFIX : GENERIC NAME ::				
PRODUCT INFO				
Dosage Form		Source Product Code		
Route Of Administration		DEA Schedule		
PACKAGING				
#	NDC	Package Description	Marketing Start Date	Marketing End Date
1		In		
INGREDIENTS				
Name (Active Moiety)		Type	Strength	
PRODUCT CHARACTERISTICS				
Characteristic	Appearance	Characteristic	Appearance	
Color		Score		
Shape		Flavor		
Imprint Text		Image		
Size				
MARKETING INFORMATION <input type="checkbox"/> Discontinued?				
Category		Application Number or Monograph	Marketing Start Date	Marketing End Date
Drug for Further Processing				

- You need to list the 1000 carton with FDA only if the bulk carton will go into commercial distribution. Commercial distribution excludes internal or interplant transfers between establishments owned by the same parent, subsidiary, and/or affiliate company. The final drug listing of the 60 and 90 count bottles should include all the establishments where any manufacturing processes have occurred.
- Ellen Wong- We also drug list our bulk packaging too. In recent discussions with FDA, we learned that the 'product code' for the bulk NDC needs to be unique than the 'product code' commercial/finished good NDC's.
- 'This is needed to properly distinguish the bulk product which is not yet packaged and labeled for dispensing/sale with the actual packaged and labeled versions that are approved.'

2. **I have a general question regarding US agent for non-US sites. For a particular site, are you allowed to have more than 1 US agent listed with FDA? I've been under the impression that you are only allowed 1 US agent per site which makes it hard come vacation time. If only one is allowed, how are you managing when that person goes on vacation?** *Susan Correia*

Howard –

- Only one US Agent. But assuming you mean how can you specify more than one contact e-mail for the US Agent, the answer is to use a group email address for the US Agent contact email (or any other contact email in the establishment registration file.)
- I don't know the technical details but a group email address is one that is shared by multiple users. When the server receives an email sent to a group email address it distributes the email to every member of the group. For example, if the US Agent was Merck and you personally were the contact you might set up an email address Susanne.usagent@merck.com which would be distributed to you and your backup.
- HOB -Out of office memo with alternate contact information
- At Bayer we use the same contact and US Agent. The FDA has always copied us both in regards to establishment questions.

[Meeting discussion:](#)

- FDA usually contacts both the company contact and the US agent.
- Do you include both the company name and person's name? No rules, FDA only checks for phone number and email number.

3. **I am hoping you can assist me with bulk finish product listing process. Do you know what happens to the SPL submission once it passes technical validation, will these NDC numbers gets posted to the NDC directory? Can this information be viewed by the industry? Any information on this process will be very helpful.** *Reena Amin*

[Meeting discussion:](#)

- Bulk SPL submissions are **not** published in the NDC directory. At this time, there is no publicly available database maintained by FDA or National Library of Medicine with those NDCs. They go into a designated database that is used by FDA imports. The validation document is proof that it is in the system.
- FDA eDRLS can provide this information if you request this, for either a labeler code or a type of listing.
- Lonnie: These types of files do not get loaded to NLM, but you can request an FOI.

4. **Hope someone can help out with a quick question. Should the description of a tablet (shape specifically) in the metadata match to how it is described in the label?** *Kerry Regan*

Meeting discussion:

- Terry - Ideally, it would. However, there is no validation rule that compares the free text in the content of labelling to the Product Data element.
- **HOB** - Since the data elements is a pick list, your tablet description falls into those categories and may not match the CMC description exactly. Remember that the EU may use different terminology than we do in the US as well so it may be difficult to standardize.

5. **I have a question regarding drug listing for a product that will be packed and labeled in a foreign facility before being shipped back to the US. (Beth Lage)**

The details are as follows:

- **Product API is manufactured at establishment A (US)**
- **Approved/OTC Drug Product manufactured Exclusively for PLD sent to be filled in another establishment B (US)**
- **shipped to a foreign facility C to be labeled and packed**
- **then shipped back to US to a distribution facility.**

The product drug listing will include establishment A,B, and C, but does establishment C need to drug list the product under its own NDC? What business operation would need to be included?

Do you know of any other customs requirements that would need to be addressed on labeling before import to US?

Here is some more information that might be helpful.

- Product API is manufactured at establishment A (US) which is the MAH holder
- sent to be filled in another establishment B (US)
- shipped to a foreign facility C to be labeled and packed
- then shipped back to US to a distribution facility.

The MAH holder would like to drug list everything (API (A), filling (B), and label and pack (C)) on the SPL with the content of labeling but knows that the foreign facility C must also drug list the product with their own NDC before importing back to the US correct? And it sounds like the distribution facility must also drug list? *Beth Lage*

Responses and Meeting Discussion:

Howard -

- If establishment A is the distributor (e.g. their name appears on the packaging as "Distributed by:") then they list as the distributor and include as establishments:

- themselves as the API manufacture,
- Establishment B as the manufacturer
- Establishment C as the labeler and packager
- There also needs to be a submission for each of the 3 establishments, Establishment A can handle all 3 listings but each listing uses the at establishment's labeler code. Establishment B lists as Drug For Further Processing and C lists using marketing category Approved/OTC Drug product Manufactured Exclusively For PLD. Establishment A's marketing category is either an approval (such as NDA) or an OTC monograph category (final or not final)
- The distribution facility (warehouse) does not have listing if all they are doing is holding the product for distribution by Establishment A. In that case they are neither a manufacturer nor a distributor.
- Question: Who should drug list the finished product?
The PLD can drug list (ie Mfg A) and will probably prefer to do this – but the regs say that the “manufacturer” is ultimately responsible for drug listing the finished product – thus Manufacturer B should be in contact with the PLD to make sure who is drug listing the finished product.

Pat:

In this case, Distributor means “labeler”. Someone (either the manufacturer or PLD) has to drug list the final finished product.

6. I have a question about EU-related SmPcs and Package Labeling Artwork being available to the public like what we have in the US via SPL format posted on DailyMed.

Audrey Anderson:

There is no European equivalent to the DailyMed in an XML format.

The longer answer is that if a product is approved via the ‘centralized procedure’ the European Medicines Association (EMA) makes the content of the labeling, including the healthcare provider labeling, patient leaflet, and packaging, available on the EMA website. For products that are approved on an individual country basis, the individual country health authorities vary in what and how the labeling is made publically available. I do not know the details for all 27(?) country health authorities. There also is an EU pharmacovigilance requirement associated with XEVMPD that may include labeling content; this is not in an XML format...yet.

The content for packaging is included in the same file as the content for the healthcare provider and patient labeling. For each product that is centrally approved, there is one large PDF file with this content. For example, for Adempas, I usually use the quick search> European public assessment report > product information > Adempas : EPAR – Product Information:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002737/human_med_001733.jsp&mid=WC0b01ac058001d124

Herb:

The European Medicines Agency announced the closure of the PIM project in 2011.

The PIM (Product Information Management) project was established to increase the efficiency of the management and exchange of product information (summary of product characteristics, package leaflet and labelling) through the structuring of the information and its exchange by electronic means.

The Agency and its partners have demonstrated significant commitment to the PIM project over the years, however the Agency is currently undertaking a review of its business strategy and information-technology system requirements in the context of new legislation and a budgetary review. As a result, it has decided to halt the PIM project.

The Agency remains committed to the concept of structured product information and the efficient exchange of information. It will return to the issue once the review process has been completed.

7. What are the regs that state that we need to submit SPL with initial submissions?

Pat: The regs say that labeling has to be submitted in SPL format. Here are the references:

21CFR314.50(l)(i) requires labeling to be submitted in electronic

format: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.50>

(i) *Labeling*. The content of labeling required under 201.100(d)(3) of this chapter (commonly referred to as the package insert or professional labeling), including all text, tables, and figures, must be submitted to the agency **in electronic format** as described in paragraph (1)(5) of this section. This requirement is in addition to the requirements of paragraph (e)(2)(ii) of this section that copies of the formatted label and all labeling be submitted.

Final guidance Providing Regulatory Submissions in Electronic Format — Content of Labeling (April 2005): **electronic means SPL**
<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072331.pdf>

This is also re-stated in the draft guidance (Oct 2009) **SPL Standard for Content of Labeling Technical Qs & As** (see lines 43-49):

<https://www.fda.gov/downloads/drugs/guidances/ucm072392.pdf>

On October 21, 2005, CDER announced in public docket number 92S-0251 that effective October 31, 2005, CDER would no longer accept content of labeling submissions in PDF format and that applicants should use the SPL standard when submitting content of labeling to FDA in XML **with original submissions, supplements, and annual reports.**

Questions for content of SPL should be directed to spl@fda.hhs.gov. Sponsors should discuss questions about content of their submission with their regulatory project manager.

Herb: Bayer submits SPL with the original submission only, and then after approval, the final SPL goes through the gateway.

8. Has anyone done more than 2 levels of NDC codes for multilevel packaging for CDER? (Ben Harpster)

Meeting responses:

Many companies do more than 2 levels of NDC codes.